

# Salvage treatment of local recurrence following radical and partial nephrectomy

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### **Purpose of review**

Standardized definition of local recurrence after radical or partial nephrectomy is still lacking. Due to its rarity, data on natural history, oncological outcomes and prognostic factors are scarce and specific treatment recommendations cannot be made.

#### Recent findings

Surgery is still the preferred option to treat a local recurrence of renal cell carcinoma, with favorable survival outcomes. However, nonsurgical options like thermal ablation techniques may represent a valid alternative mainly in patients where a nephron-sparing treatment is imperative. Systemic therapy seems to have a limited role in this setting.

#### Summary

According to available data, surgical excision of local recurrence should be attempted whenever feasible. Alternatively, thermal ablation represents a reliable and repeatable option after partial nephrectomy, with low complication rate and good oncologic outcomes. However, the evidence comes mainly from limited, heterogeneous case series. Further high-quality studies are needed to properly define the most appropriate for each individual patient.

#### **Keywords**

local recurrence, partial nephrectomy, radical nephrectomy, renal cell carcinoma, survival

#### INTRODUCTION

Renal cell carcinoma (RCC) accounts for 2.2% of all cancer diagnoses worldwide [1]. Over the last two decades, RCC incidence rates has been estimated to increase by 2% in both Europe [2] and North America [3]. Although a stage migration phenomenon towards early stages has been seen, also locally advanced and metastatic RCCs showed a marginal increase [3]. Surgery is the mainstay treatment for nonmetastatic RCCs. Based on current guidelines, partial nephrectomy (PN) is the preferred treatment for clinically localized RCCs [4–6]. Conversely, radical nephrectomy (RN) is the preferred treatment for locally advanced tumors [4].

Local recurrence (LR) in the renal fossa or in the residual renal parenchyma after RN or PN may occur [7]. Due to its rarity, data on natural history, oncological outcomes and prognostic factors of LR are scarce. Consequently, treatment strategies and specific recommendations can hardly be made [4]. Given this challenging clinical scenario, we reviewed the available literature on the management of LR after either PN or RN, assessing definitions of LR, treatment options and related outcomes and prognostic factors.

# **DEFINITION OF LOCAL RECURRENCE AFTER SURGERY**

Traditionally, LR after RN is defined as "tumor growth exclusively confined to the true renal fossa" while LR after PN is defined as "tumor growth at the site of the primary treatment within the kidney". However, the definition of LR widely varies and no standardized definition can be currently recognized, making estimation of the true incidence of LR difficult. Especially in case of conservative treatment, recent literature focused on the distinction between recurrence in the same kidney outside the resection bed (metachronous lesion) vs. persistence of disease in the resection bed or in the area treated by thermal

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**Curr Opin Urol** 2025, 35:481–488 DOI:10.1097/MOU.0000000000001286

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ablation, as the former represents a new oncologic event while the latter a treatment failure [8].

Standardized definitions of LR after PN have been proposed. Antonelli et al. [9] analyzed 18 cases of relapse after PN subsequently treated with salvage RN. They assessed the pathological features of the tumor-parenchyma interface at the time of PN and of the resection bed at the time of salvage surgery and identified three types of LR. Specifically, type A had a mixture of cancer cells and granulomatous reaction at the resection bed, due to incomplete tumor resection at first surgery; type B had diffuse microvascular embolization and relapse in the same portion of the kidney of the primary tumor; type C had relapsing tumors located in distinct portions of the kidney. Notably, only three patients had positive surgical margins (PSMs) at the time of PN. Of these, only one patient had type A LR, suggesting that PSM status itself is poorly related to the likelihood of a LR. This finding was further confirmed by Bertolo et al. [10], who evaluated a cohort of 30 patients clinically diagnosed with LR. The authors divided LRs into three groups: group 1 – true development of a LR of the previously resected RCC; group 2 – new occurrence of RCC, with new foci of RCC unrelated to the previously resected one; group 3 – micrometastatic RCC. PSM status was poorly related to the likelihood of a true LR [11].

A new classification system based on the specific location and number of recurrences has been developed [12]. Using data from the ASSURE trial, the authors described a novel four-tier anatomical classification system that defines recurrences as follows: type I – single recurrence in a remnant kidney or ipsilateral renal fossa; type II – single recurrence in the ipsilateral vasculature, the ipsilateral adrenal gland or a lymph node; type III – single recurrence in other intra-abdominal soft tissues or organs; type IV – any combination of types I–III or multiple recurrences of a single type. Out of 1943 patients in this series, 300 (15.4%) had LR, of whom 22% had type I, 32.3% type II, 29% type III and 16.7% type IV. Survival analyses showed 5-year cancer specific survival and overall survival were worse in patients with type IV recurrence (P < 0.001), while there was no difference in survival among patients with type I to III recurrence. Additionally, authors assessed predictors of LR. Only pathological features such as larger tumor size, lymph node invasion, presence of tumor necrosis, sarcomatoid features and vascular invasion were independent predictors of LR. Conversely, age, surgery type (PN vs. RN) and surgical modality (minimally-invasive vs. open surgery) did not predict LR. These data showed that LR seems to mainly depend on tumor biology rather than on surgical technique or approach. The authors

highlight the need for a standardized definition of LR, as well as the importance of considering the presence of multiple LRs as a separate condition, due to their worse prognosis.

# SALVAGE TREATMENT AFTER PARTIAL NEPHRECTOMY

### Salvage surgery

Management options for recurrent RCC after PN include RN, thermal ablation (TA) techniques and repeat PN (Table 1). Although RN is associated with the best oncological control, its efficacy must be balanced with the negative effects on renal function. This is particularly important for patients with a solitary kidney or with an impaired renal function. Du et al. reported a median overall survival (OS) and CSS of 34.4 and 35.4 months respectively for recurrent RCCs after PN treated with RN, with a nonstatistically significant difference compared to patients of the same cohort who recurred after RN [13]. Most published studies, including the largest cohort [14], report on open repeat PN, including mainly VHL patients. Other cohorts include patients with a solitary kidney, where the indication for nephron-sparing surgery (NSS) can be considered imperative [15]. Overall, the reported oncologic outcomes are acceptable, with a 100% OS rate after a median follow-up of 56 months and a 95% metastasis-free survival (MFS) rate at a median follow-up of 50 months in Johnson et al. and Liu et al. study, respectively. The majority of patients maintained an adequate renal function and only 2-3 of them needed dialysis during follow-up [14,15]. Perioperative complication rate was 19.6% vs. 52%, with pleural injury and urinary leak being the most frequent complications reported by Johnson and Liu et al. respectively. Median estimated blood loss (EBL) was 1800 vs 2400 ml with a 64% vs. 76% transfusion rate [14,15]. These data clearly indicate a high overall complication rate, but the oncologic outcomes are acceptable and the decrease in renal function is modest, with most patients avoiding dialysis. When multiple resections are performed on the same renal unit, data are comparable to those reported by Johnson et al. and Liu et al. showing that repeat salvage PN is feasible in experienced hands [16].

The use of robotic technology is associated with complication rates that are comparable to those reported for repeat open PN series [17]. Autorino *et al.* reported no intraoperative and only 2 minor postoperative complications in a cohort of robot-assisted partial nephrectomy (RAPN) patients. Median EBL was 150 ml, which is comparable to that of patients treated for a primary RCC. This

**Table 1.** Studies reporting on perioperative, functional and oncological outcomes of repeat partial nephrectomy for local renal cell carcinoma recurrence after partial nephrectomy

	Pts (n)	Lesions (n)	Approach	Survival	Median eGFR change (ml/min)	Pts needing dialysis (n)	Conversion to RN (n)	Median EBL (ml)	Transfusion rate (%)	Major complications (%)
Johnson et al. J Urol, 2008	47	51	Open 3 Laparoscopic	OS 100% after 56 months	- 10 <i>.</i> 7	2	3	1800	64	Perioperative: 19.6% 1 perioperative death
Liu et al. J Urol, 2010	25	25	Open	MFS 95% after 50 months	-4	3	3	2400	76	Perioperative: 52% 1 perioperative death
Bratslavsky et al. J Urol, 2008	11	13	Open	OS 100% MFS 100% after 25 months	-16	2	3	2100	23	Perioperative: 46%
Watson et al. J Endourol, 2016	26	26	Robotic	NA	-5.2	0	0	900	19.2	Overall complications: 57.7% Conversion to open: 15.4%
Autorino et al. BJU Int, 2013	9	9	Robotic	OS 100% after 8.3 months	<b>−7</b>	0	0	150	0	No intraoperative complications 2 minor postoperative complications

MFS, metastasis-free survival; NA, not applicable; OS, overall survival; RN, radical nephrectomy.

may be due to the low number of patients enrolled [18].

Studies show that repeat PN for local RCC recurrence is technically feasible, but is associated with higher morbidity compared to primary PN, even when using a minimally invasive approach. A nonnegligible risk of renal unit loss exists. However, repeat PN provides an acceptable cancer control and most patients preserve a sufficient renal function to avoid dialysis.

#### Thermal ablation

Thermal ablation techniques [mainly radiofrequency ablation (RFA) and cryoablation (CA)] may represent a valid, less invasive alternative to surgery, especially in patients where the indication for a nephron-sparing treatment is imperative (Table 1, Supplemental Digital Content, http://links.lww. com/COU/A62). Monfardini et al. showed RFA to be an effective treatment with OS and DFS of 100% and 62% respectively, at a median follow-up of 12 months [19]. Longer follow-up was reported by other authors with similar outcomes: OS and CSS were 92% and 100% at a median follow-up of 37.6 months after RFA or CA in the series of Yang et al. [20], while Hegg et al. reported a 5 years OS and RFS of 84% and 73%, respectively, after CA [21]. In patients with a secondary recurrence, TA was repeated. The treatment was successful in all cases, thereby showing that ablative therapies can be repeated with good outcomes.

TA techniques are associated with low perioperative complication rates. Yang *et al.* reported no complications [20]. Three major complications (5.7%) were described by Hegg *et al.* which is comparable to the 7.7% major complication rate reported by Atweel *et al.* in a review of CAs performed for primary RCCs [21,22]. A median eGFR decrease of 1.5 ml/min was reported by Hegg [21], whereas in Yang *et al.* cohort the estimated glomerular filtration rate (eGFR) decreased from a preprocedural 61 ml/min to a postprocedural 51.7 ml/min. No patients developed chronic kidney disease or required dialysis [20].

TA techniques represent a viable, repeatable treatment for patients with local RCC recurrence after PN, as they are associated with low complication rates, minimal decrease in renal function and acceptable oncologic outcomes.

# SALVAGE TREATMENT AFTER RADICAL NEPHRECTOMY

## Salvage surgery

Although few retrospective series including small and heterogeneous populations are available, there is evidence that radical excision of local recurrence, whenever technically feasible, can improve survival (Table 2). In one of the largest series reported, Margulis *et al.* analyzed the outcomes and predictive factors in a group of 54 M0 RCC patients surgically treated for a local recurrence. At multivariable

**Table 2.** Studies reporting on perioperative and oncological outcomes of open surgery for local renal cell carcinoma recurrence after radical nephrectomy

	Pts (n)	DMTT (n)	Relapse size (cm)	Median time from RN to recurrence (mo.)	pTN (n)	Recurrence site	Additional therapy (n)	CSS (mo.)	PFS (mo.)	Risk factors for survival	Complications
Schrodter et al. J Urol, 2002	13	0	5.9	45.5	T1 (1) T2 (4) T3 (6) T4 (2) N+ (1)	Renal fossa	Adjuv. (4)	52.4	-	Shorter time to recurrence Recurrence size	0
Margulis et al. J Urol, 2009	54	0	6.0	10	T1 (10) T2 (11) T3 (33) N+ (11)	Renal fossa, adrenal gland, regional lymph nodes	Neoad. (21) Adjuv. (10) Neoad. + Adjuv. (6)	61	11	PSM Recurrence size Sarcomatoid features	Grade III-IV (8) Grade V (2)
Thomas et al. J Urol, 2015	102	4	4.5	19	T1 (20) T2 (20) T3 (59) T4 (1) N+ (20)	Renal fossa, adrenal gland, psoas muscle, regional lymph nodes	Neoad. (46) Adjuv. (48)	66	23	pN+ at RN Recurrence size	Grade III-IV (13) Grade V (2)
Du et al. Clin Genitourin Cancer, 2016	44	-	4.5	29.8	-	Renal fossa, adrenal gland, regional lymph nodes	-	-	-	Shorter time to recurrence Recurrence size	-

Adjuv, adjuvant; CSS, cancer-specific survival; DMTT, distant metastases at time of treatment; mo., months; Neoad, neoadjuvant; PFS, progression-free survival; RN, radical nephrectomy.

analysis, PSMs after resection of the local recurrence, recurrence tumor size and sarcomatoid features in the recurrence specimen were independently associated with the risk of cancer-specific death. The site of recurrence (renal fossa vs ipsilateral adrenal gland vs. regional lymph nodes) did not independently predict CSS. The authors proposed a stratification of patients into low vs intermediate vs high risk of dying from cancer by using a prognostic risk model based on the number of the above mentioned risk factors: patients with 0, 1 and > 1 factors had a CSS of 111, 40, and 8 months, respectively [23\*\*].

In a series reported by Thomas *et al.* 3 and 5 years CSS rates were 71% and 52%. At multivariate analysis, authors reported pN+ stage at the time of RN and maximum diameter of the local recurrence as independent predictors for CSS [24\*\*], whereas Du *et al.* showed that recurrence size < 7 cm and time to local recurrence > 24 months were associated with longer CSS [13].

In a retrospective multicenter study including M0 patients with local retroperitoneal recurrence after RN, the authors compared the outcomes of surgery vs. targeted therapy alone. Surgical treatment was associated with a significantly longer CSS. At multivariable analysis, high Fuhrman grade, local recurrence size, mixed type of recurrence, multiple recurrent lesions and the absence of surgery were associated with a significantly increased risk of death [25].

The role of local treatment of recurrence in a homogeneous population was assessed in a series of 97 patients with relapse after RN or PN. At multivariable analysis, local treatment, low- vs. high-risk risk recurrence and the absence of extra-abdominal/thoracic metastasis were significant predictors of longer OS. Moreover, the effect of local treatment on survival was consistent across all risk groups [26\*\*].

Despite historical studies reported a high risk of perioperative complications, more recent case series show an acceptable morbidity profile. Clavien grade 3–4 complications occurred in 14.8% and 12.7% patients in Margulis and Thomas study, with 2 perioperative deaths in each series [23\*\*\*,24\*\*\*].

Two studies specifically enrolled patients with isolated nodal recurrence after RN (Table 2, Supplemental Digital Content, http://links.lww.com/COU/A63), showing that median PFS and CSS were comparable to those of N+M0 patients at the time of RN [27,28].

The available evidence supports the role of aggressive surgery for the treatment of isolated retroperitoneal RCC recurrence, as it improves survival. Time from RN to detection of local recurrence and recurrence size are the most frequently reported independent predictors of survival. This underlines the importance of a strict follow-up imaging in high-risk patients in order to detect local recurrences at an early stage, where surgical resection is possible.

## Minimally invasive surgery

The feasibility of laparoscopic management of local recurrences has been described in small case series (Table 3). In their series, Bandi *et al.* reported one out of five conversions to open surgery and no

**Table 3.** Studies reporting on perioperative and oncological outcomes of laparoscopic/robotic surgery for local renal cell carcinoma recurrence after radical nephrectomy

	Pts (n)	DMTT (n)	Relapse size (cm)	Median time from RN to recurrence (mo.)	pTN ( <i>n</i> )	Recurrence site	Additional therapy (n)	CSS (mo.)	PFS (mo.)	Complications (n)
Bandi et al. Urology, 2008	5	NA	4.9	23	T1 (2) T3 (3) N+ (0)	Renal fossa	Adjuv. (1)	60% at median follow-up 43 mo.	20% at median follow-up 43 mo.	0
Yohannan et al. J Endourol, 2010	4	0	5.7	11.5	T1 (1) T2 (2) T3 (1) N+ (0)	Adrenal gland, regional lymph nodes	Neoad. (1)	-	75% at median follow-up 12 mo.	Diaphragm injury (1)
Sanli et al. JSLS, 2012	5	1	3.3	51.2	T1 (3) T2 (1) T4 (1) N+ (0)	Renal fossa, psoas muscle	Adjuv. (2) Neoad. (3)	100% at median follow-up 8.4 mo.	60% at median follow-up 8.4 mo.	Pleural injury (1)
El Hajj et al. BJU Int, 2013	9	0	3.4	83	Tx (3) T1 (3) T2 (1) T3 (2) N+ (1)	Renal fossa, adrenal gland, regional lymph nodes, liver infiltration	Adjuv. (2) Neoad. (3)	1 cancer- related death at median follow-up 3 years	67% at median follow-up 3 years	Diaphragm injury (2) Pleurisy (1)

Adjuv, adjuvant; CSS, cancer-specific survival; DMTT, distant metastases at time of treatment; mo., months; NA, not applicable; Neoad, neoadjuvant; PFS, progression-free survival; RN, radical nephrectomy.

perioperative complications [29]. No open conversions were reported by Yohannan *et al.* in four patients with only one significant intraoperative complication [30]. A CSS and DFS of 100% and 60% and of 89% and 67% respectively were reported by Sanli *et al.* and El Hajj *et al.* suggesting that the laparoscopic approach may be comparable to open surgery for selected low-volume recurrences [31,32].

In the first reported experience of robot-assisted surgery in this field, Gilbert and Abaza described 3 patients with an isolated 1.5–2 cm RCC recurrence in the renal fossa or the retroperitoneal lymph nodes. Neither complications nor open conversions occurred and no further recurrences were detected after surgical treatment [33].

# Intraoperative radiation therapy

Radiation therapy has been advocated as a reasonable and effective local therapy in addiction to surgery either in the intraoperative or adjuvant setting. However, the relatively low sensitivity of RCC to radiations and the risk of additional toxicity have limited its applicability in clinical practice.

Studies reported the use of intraoperative radiation therapy (IORT) in the treatment of RCC local recurrence after RN, with controversial results (Table 3, Supplemental Digital Content, http://links.lww.com/COU/A64). Master *et al.* reported 6 (60%) deaths among patients who received IORT compared to 3 (75%) among those who received only surgery. IORT did not provide a survival benefit [34]. Multimodal treatment with a combination of surgery, intraoperative electron radiation therapy

(IOERT) and external beam radiation therapy (EBRT) resulted in high local control rates (91% at 2 years) with low toxicity in a study by Habl *et al.* despite a high metastatic progression rate (PFS of 32% at 2 years) [35]. In the largest series published, a higher radiation dose was significantly associated with decreased OS and CSS. Additionally, patients who received adjuvant systemic therapy showed decreased CSS [36]. Selection criteria for radiation treatment are not well defined and outcomes are controversial. No comparisons with surgery alone are reported.

# Nonsurgical treatment (thermal ablation, radiation therapy, systemic therapy)

RCC radio-resistance has historically limited the role of EBRT to palliation of symptoms of the primary renal tumor or metastases. However, stereotactic body radiotherapy (SBRT) with high dose in few fractions has been shown to overcome that resistance [37]. Retrospective analysis including mainly pT3 RCCs showed better 5-year DFS for patients who underwent adjuvant RT after RN [38]. Although to date there are no studies assessing the survival benefit of SBRT in the setting of local RCC recurrence, results from patient cohorts with primary or metastatic RCC suggest that SBRT should be considered in selected cases in which surgery is not an option. Monfardini et al. evaluated the role of RFA for management of retroperitoneal nodal recurrences showing favorable short-term outcomes [19].

Systemic therapy has been used in a neoadjuvant or adjuvant setting, but not as a stand-alone therapy, without a standardized schedule. Santoni et al. showed no statistically significant PFS difference for sunitinib vs. sorafenib vs. pazopanib [39]. Other authors used targeted therapy to downsize the local recurrence in order to enhance the oncological outcomes of local treatment. Brehmer et al. reported a 67 and 12 months OS and DFS, respectively, in patients treated with either sunitinib, pazopanib, bevacizumab or temsirolimus. Neoadjuvant targeted therapy was associated with a successful complete local treatment in approximately 70% of patients [40].

## **Comparative studies**

Most studies report on single specific treatment options and few comparative studies have been published with heterogeneous cohorts (Table 4). Itano et al. showed that patients who underwent surgery for local RCC recurrence had a 5-year CSS rate of 51% compared to 18% of patients treated with adjuvant medical therapy alone and 13% with observation alone [41]. Similarly, Bruno et al. showed that surgical resection gives a survival advantage to patients with an isolated local recurrence after RN and should be attempted whenever

possible. Conversely, patients with synchronous metastatic disease will not benefit from surgery and should be considered for systemic therapy [42\*]. In a multiinstitutional study of patients treated with surgery alone vs. systemic therapy alone (sunitinib, sorafenib or bevacizumab) vs. multimodal therapy (surgery plus systemic therapy) vs. best supportive care [43\*], the lack of surgical treatment was significantly associated with cancerspecific mortality, together with a shorter time to recurrence, in keeping with other studies [13,28,35]. Patients who received a wide variety of treatment combinations were distinguished by Psutka et al. in three groups: locally directed treatment (surgery, thermal ablation, radiotherapy) vs. systemic therapy vs. observation. CSS rate at 3 years was significantly superior in the first group [44].

In conclusion, comparative studies support the primary role of locally directed therapies, mainly surgery, over systemic treatment, based on better survival outcomes. Surgical excision of local recurrence should therefore be considered as the first treatment choice whenever feasible.

#### CONCLUSION

Local recurrence after radical or partial nephrectomy is a rare condition. A standardized definition

Table 4. Comparative studies reporting on perioperative and oncological outcomes of different treatments for local renal cell carcinoma recurrence after radical nephrectomy

	Pts (n)	DMTT (n)	Relapse size (cm)	Median time from RN to recurrence (mo.)	pTN (n)	Recurrence site	Treatments	CSS (median or mo.)	Risk factors for survival
Bruno et al. BJU Int, 2006	34	16	3.8	17	T1 (8) T2 (5) T3 (14) T4 (6) N+ (0)	Renal fossa, adrenal gland, regional lymph nodes	Surgery (16) Nonsurgical treatment (18)	Surgery for M0 (71.4 mo.) Nonsurgical treatment for M0 (9.9 mo.) Surgery for M+ (16.3 mo.) Nonsurgical treatment for M+ (11.8 mo.)	Better CSS with surgery in the absence of metastasis
Itano et al. J Urol, 2000	30	0	-	34	T1-2 (13) T3 (17) N+ (0)	Renal fossa	Surgery ± adjuvant ST (10) Nonsurgical therapy (11) Observation (9)	Surgery 51% ST 18% Observation 13% at 5 years	Better CSS with surgery
Paparel et al. J Surg Oncol, 2014	72	23	4.7	26.5	Tx (2) T1 (21) T2 (13) T3 (32) T4 (4) N+ (16)	Renal fossa, adrenal gland, regional lymph nodes	Surgery (24) ST (18) Surgery + ST (24) Palliation (6)	46% at 5 years	Short time to recurrence (< 1 year) Better CSS with surgery
Psutka et al. BJU Int, 2017	63	30	-	1.4 years	-	Renal fossa	14 different combinations of: surgery, thermal ablation, EBRT, IORT, ST, observation	Local therapy (64%) ST (50%) Observation (28%)	Better CSS with locally directed therapies

CSS, cancer-specific survival; DMTT, distant metastases at time of treatment; EBRT, external beam radiation therapy; IORT, intraoperative radiation therapy; mo., months; RN, radical nephrectomy; ST, systemic therapy.

clearly distinguishing different types of local relapse with potential different prognosis is lacking. The current evidence in this field is scarce and comes from case reports or limited case series, with the optimal treatment of local recurrence not yet defined. Overall, when feasible surgical resection is the preferred option with better reported outcomes, but nonsurgical alternatives are possible especially in imperative conditions. Systemic therapy may have a role in a neoadjuvant or adjuvant setting. High quality studies are needed to properly define the most appropriate therapy for each individual patient.

### Acknowledgements

None.

# Financial support and sponsorship

None.

#### **Conflicts of interest**

There are no conflicts of interest.

# REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest
- Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68:394–424.
- Capitanio U, Bensalah K, Bex A, et al. Epidemiology of renal cell carcinoma. Eur Urol 2019; 75:74–84.
- Palumbo C, Pecoraro A, Knipper S, et al. Contemporary age-adjusted incidence and mortality rates of renal cell carcinoma: analysis according to gender, race, stage, grade, and histology. Eur Urol Focus 2021; 7:644–652.
- Ljungberg B, Albiges L, Abu-Ghanem Y, et al. European Association of Urology guidelines on renal cell carcinoma: the 2019 update. Eur Urol 2019; 75:799–810.
- Motzer RJ, Jonasch E, Michaelson MD, et al. NCCN guidelines insights: kidney cancer, version 2.2020. J Natl Compr Canc Netw 2019; 17:1278– 1285.
- Campbell S, Uzzo RG, Allaf ME, et al. Renal mass and localized renal cancer: AUA guideline. J Urol 2017; 198:520–529.
- Kriegmair MC, Bertolo R, Karakiewicz PI, et al. Systematic review of the management of local kidney cancer relapse. Eur Urol Oncol 2018; 1:512–523.
- Martini A, Turri F, Barod R, et al. Salvage robot-assisted renal surgery for local recurrence after surgical resection or renal mass ablation: classification, techniques, and clinical outcomes. Eur Urol 2021; 80:730–737.
- Antonelli A, Furlan M, Tardanico R, et al. Features of ipsilateral renal recurrences after partial nephrectomy: a proposal of a pathogenetic classification. Clin Genitourin Cancer 2017; 15:540–547.
- Bertolo R, Nicolas M, Garisto J, et al. Low rate of cancer events after partial nephrectomy for renal cell carcinoma: clinicopathologic analysis of 1994 cases with emphasis on definition of "recurrence". Clin Genitourin Cancer 2019; 17:209–215; e1.
- 11. Hakam N, Abou Heidar N, Khabsa J, et al. Does a positive surgical margin after nephron sparing surgery affect oncological outcome in renal cell carcinoma? a systematic review and meta-analysis. Urology 2021; 156:e30–e39.
- Lee Z, Jegede OA, Haas NB, et al. Local recurrence following resection of intermediate-high risk nonmetastatic renal cell carcinoma: an anatomical classification and analysis of the ASSURE (ECOG-ACRIN E2805) Adjuvant Trial. J Urol 2020; 203:684–689.
- Du Y, Grüllich C, Hadaschik B, et al. Local recurrence after curative surgical treatment of renal cell cancer: a study of 91 patients. Clin Genitourin Cancer 2016; 14:e379–e385.

- Johnson A, Sudarshan S, Liu J, et al. Feasibility and outcomes of repeat partial nephrectomy. J Urol 2008; 180:89–93; discussion 93.
- Liu NW, Khurana K, Sudarshan S, et al. Repeat partial nephrectomy on the solitary kidney: surgical, functional and oncological outcomes. J Urol 2010; 183:1719–1724.
- Bratslavsky G, Liu JJ, Johnson AD, et al. Salvage partial nephrectomy for hereditary renal cancer: feasibility and outcomes. J Urol 2008; 179:67–70.
- Watson MJ, Sidana A, Diaz AW, et al. Repeat robotic partial nephrectomy: characteristics, complications, and renal functional outcomes. J Endourol 2016; 30:1219–1226.
- Autorino R, Khalifeh A, Laydner H, et al. Repeat robot-assisted partial nephrectomy (RAPN): feasibility and early outcomes. BJU Int 2013; 111:767–772.
- Monfardini L, Varano GM, Foà R, et al. Local recurrence of renal cancer after surgery: prime time for percutaneous thermal ablation? Cardiovasc Intervent Radiol 2015; 38:1542–1547.

This study shows how radiofrequency ablation may be a reliable alterative for the treatment of a local recurrence of RCC after surgery. Thermal ablation techniques should therefore be considered especially in patients where indication to a nephron-sparing approach is imperative.

- Yang B, Autorino R, Remer EM, et al. Probe ablation as salvage therapy for renal tumors in von Hippel-Lindau patients: the Cleveland Clinic experience with 3 years follow-up. Urol Oncol 2013; 31:686–692.
- Hegg RM, Schmit GD, Boorjian SA, et al. Percutaneous renal cryoablation after partial nephrectomy: technical feasibility, complications and outcomes. J Urol 2013; 189:1243–1248.
- Atwell TD, Carter RE, Schmit GD, et al. Complications following 573
  percutaneous renal radiofrequency and cryoablation procedures. J Vasc
  Interv Radiol 2012; 23:48–54.
- 23. Margulis V, McDonald M, Tamboli P, et al. Predictors of oncological outcome
  after resection of locally recurrent renal cell carcinoma. J Urol 2009;
- after resection of locally recurrent renal cell carcinoma. J Urol 2009; 181:2044–2051.
  In this study authors analysed predictive factors for cancer-specific death of

patients with local recurrence surgically treated. Consequently they proposed a stratification of patients according to the risk of dying from cancer. This prognostic model could be helpful in scheduling the follow-up of these patients.

Thomas AZ, Adibi M, Borregales LD, et al. Surgical management of local retroperitoneal recurrence of renal cell carcinoma after radical nephrectomy. J Urol 2015; 194:316–322.

This is one of the largest series reported, showing pN+ stage at the time of RN and maximum diameter of recurrence as independent predictors for CSS. This evidence may be of use to properly follow-up specific high-risk patients.

- Huang J, Wang Y, Zhang C, et al. Surgical management and oncologic outcomes for local retroperitoneal recurrence of renal cell carcinoma after radical nephrectomy. Clin Genitourin Cancer 2023; 21:315e1–315e7.
- 26. Marconi L, Kuusk T, Capitanio U, et al. Local treatment of recurrent renal cell
- carcinoma may have a significant survival effect across all risk-of-recurrence groups. Eur Urol Open Sci 2023; 47:65–72.

This is one the most recent studies on the topic. Most importantly, it shows the role of local treatment of RCC relapse in selected patients in a homogeneous population.

- Boorjian SA, Crispen PL, Lohse CM, et al. Surgical resection of isolated retroperitoneal lymph node recurrence of renal cell carcinoma following nephrectomy. J Urol 2008; 180:99–103; discussion 103.
- Russell CM, Lue K, Fisher J, et al. Oncological control associated with surgical resection of isolated retroperitoneal lymph node recurrence of renal cell carcinoma. BJU Int 2016; 117(6B):E60–66.
- Bandi G, Wen CC, Moon TD, Nakada SY. Single center preliminary experience with hand-assisted laparoscopic resection of isolated renal cell carcinoma fossa recurrences. Urology 2008; 71:495–499; discussion 499– 500
- Yohannan J, Feng T, Berkowitz J, et al. Laparoscopic resection of local recurrence after previous radical nephrectomy for clinically localized renalcell carcinoma: perioperative outcomes and initial observations. J Endourol 2010; 24:1609–1612.
- **31.** Sanli O, Erdem S, Tefik T, *et al.* Laparoscopic excision of local recurrence of renal cell carcinoma. JSLS 2012; 16:597–605.
- El Hajj A, Thanigasalam R, Molinié V, et al. Feasibility and oncological outcomes of laparoscopic treatment for local relapse of renal cell carcinoma. BJU Int 2013; 112:E307–313.
- Gilbert D, Abaza R. Robotic excision of recurrent renal cell carcinomas with laparoscopic ultrasound assistance. Urology 2015; 85:1206–1210.
- Master VA, Gottschalk AR, Kane C, Carroll PR. Management of isolated renal fossa recurrence following radical nephrectomy. J Urol 2005; 174:473–477; discussion 477.
- Habl G, Uhl M, Hensley F, et al. Intraoperative electron radiation therapy (IOERT) in patients with locally recurrent renal cell carcinoma. Radiat Oncol 2013; 8:282.
- Paly JJ, Hallemeier CL, Biggs PJ, et al. Outcomes in a multiinstitutional cohort of patients treated with intraoperative radiation therapy for advanced or recurrent renal cell carcinoma. Int J Radiat Oncol Biol Phys 2014; 88:618–623.
- **37.** De Meerleer G, Khoo V, Escudier B, *et al.* Radiotherapy for renal-cell carcinoma. Lancet Oncol 2014; 15:e170–e177.

- Ulutin HC, Aksu G, Fayda M, et al. The value of postoperative radiotherapy in renal cell carcinoma: a single-institution experience. Tumori 2006; 92:202–206.
- Santoni M, Conti A, Porta C, et al. Sunitinib, pazopanib or sorafenib for the treatment of patients with late relapsing metastatic renal cell carcinoma. J Urol 2015; 193:41–47.
- Brehmer B, Kauffmann C, Blank C, et al. Resection of metastasis and local recurrences of renal cell carcinoma after presurgical targeted therapy: probability of complete local control and outcome. World J Urol 2016; 34:1061–1066.
- Itano NB, Blute ML, Spotts B, Zincke H. Outcome of isolated renal cell carcinoma fossa recurrence after nephrectomy. J Urol 2000; 164: 322–325.
- **42.** Bruno JJ, Snyder ME, Motzer RJ, Russo P. Renal cell carcinoma local recurrences: impact of surgical treatment and concomitant metastasis on
- survival. BJU Int 2006; 97:933–938. This study highlights the importance of surgery as the preferred treatment choice in case of isolated local recurrence after RN.
- 43. Paparel P, Bigot P, Matillon X, et al. Local recurrence after radical nephrectomy for kidney cancer: management and prediction of outcomes. a multi-institutional study. J Surg Oncol 2014; 109:126–131.
- This study further highlights the importance of surgery as the preferred treatment choice in case of isolated local recurrence after RN.
- Psutka SP, Heidenreich M, Boorjian SA, et al. Renal fossa recurrence after nephrectomy for renal cell carcinoma: prognostic features and oncological outcomes. BJU Int 2017; 119:116–127.